Restless legs syndrome among women with Chronic Widespread Pain

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I. Stehlik R, Arvidsson L, Ulfberg J
Restless legs syndrome is common among female patients with fibromyalgia.
Eur Neurol. 2009; 61(2): 107-11

II. Stehlik R, Hedner J, Ulfberg J, Grote L
High prevalence of restless legs syndrome among women with multi-site pain: a population-based study in Dalarna, Sweden.
Eur J Pain. 2014; 18(10): 1402-9

III. Stehlik R, Ulfberg J, Ding Z, Hedner J, Grote L
Restless Legs Syndrome and pain deteriorate daytime sleepiness, body fatigue and sleep - a population based survey.
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III. Stehlik R, Ulfberg J, Hedner J, Grote L
Incidence of Restless Legs Syndrome in females with chronic widespread pain and the associations with sleep, mood, and biomarkers.
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ABSTRACT

Aims: The main aim of this thesis was to explore the prevalence, incidence and severity of Restless Legs Syndrome (RLS) in subjects with Chronic Widespread Pain (CWP). In addition, the thesis aimed to analyse the impact of pain and RLS on sleep as well as on measures of Hypothalamic–Pituitary–Adrenal (HPA)-axis function and skin sympathetic activity.

Methods: Study I: In this cross-sectional cohort study 232 patients with fibromyalgia (FMS) answered a questionnaire on RLS symptoms and sleep quality. Studies II and III: Females in the age range 18-65 years were randomly recruited from the general population in Dalarna county (final analysis cohort n=3060 in study II and n=2727 in study III, respectively). Participants answered questions on A) the quality, quantity and spreading of pain and B) the occurrence of RLS based on established diagnostic criteria (study II). In study III, the independent influences of RLS and pain spreading on sleep quality and daytime symptoms like sleepiness and body fatigue were analysed. Study IV: In a longitudinal study, subjects with (n=27 cases) and without widespread pain (n=27 controls) were randomly recruited 2 years after entry in studies II/III. Prevalence and incidence of RLS, pain, and occurrence of depressive symptoms were captured. Morning cortisol and fasting glucose concentrations were analysed. A sleep study addressing sleep disordered breathing and skin sympathetic activity using finger pulse wave amplitude (PWA) analysis was performed.

Results: Study I; The prevalence of RLS in women with FMS was high (64%) and difficulties initiating sleep were more prevalent in FMS patients with RLS compared with FMS patients without RLS (49% vs. 32%, p=0.01). Study II; There was a linear relationship between pain spreading and RLS, the prevalence of RLS was 10% in subjects with no reported pain and 24% and 55% in those reporting 1 and 5 pain areas, respectively ($p<0.001$) and this association was independent of cofounders like age, body mass index, and psychiatric disease. Study III; Intensity and spreading of pain as well as RLS diagnosis were all independently associated with impaired quantity and quality of sleep ($p<0.001$). The occurrence of daytime sleepiness increased with both pain spreading and RLS diagnosis ($p<0.001$) but only pain spreading predicted body fatigue ($p<0.001$). Study IV; The two-year RLS incidence was higher in those with CWP (n=12) compared with controls without CWP (n=2). In subjects with CWP, morning cortisol (464±141 vs. 366±111 nmol/l, p=0.011) and finger vasoconstriction events during sleep (PWA 50% 11.2±8 vs. 6.1±2 events/hour, p=0.048) were elevated compared with controls suggesting an activated HPA axis and sympatico-adrenal system in subjects with CWP. However, RLS status did not influence those parameters.

Conclusions: RLS is highly prevalent in females with CWP. Our data suggest that CWP may trigger RLS development. Both CWP and RLS have a deteriorating effect on sleep quality and daytime sleepiness. Comorbid anxiety and depression were frequently present in both CWP and RLS. Further analysis suggests that CWP is associated with activations of both the HPA axis and the sympathetic system, which may influence the development of RLS.

Keywords: Chronic Widespread Pain, Restless Legs Syndrome, Females, Sleep Disorders, HPA-axis

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